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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/441,061	11/16/1999	JOSEF ENDI	P564-9035	3812

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EXAMINER	
DECLOUX, AMY M	

ART UNIT	PAPER NUMBER
1644	15

DATE MAILED: 01/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/441,061	Applicant(s) ENDI ET AL.	
	Examiner Amy M. DeCloux	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-79* is/are pending in the application.

4a) Of the above claim(s) *59-79* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *46-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 November 1999* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 46-58 as applied to SEQ ID NO:2 in Paper No. 6 and 11, filed 11-13-01 and 4-29-02, respectively, is acknowledged. The traversal is on the ground(s) that the amino acid sequences of SEQ ID NO:2, 3 and 19-39 exhibit common technical features in that they are derived from GAD65 and bind to MHC-II molecules of the type DR3 or DR4. This is not found persuasive because each sequence has a distinct structure, as well as distinct biophysical properties, including a distinct ability to bind to distinct MHC-II molecules. Consequently the search for each of the SEQ ID NO:s is not coextensive with a search for the remaining SEQ ID NO:s. MPEP 803 states that: "For the purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation, either separate classification, separate status in the art, or different field of search. Because a search in the non-patent literature for all the SEQ ID NO:s are not coextensive, an examination and search of all said SEQ ID NO:s in a single application would constitute a serious undue burden on the Examiner, restriction for examination purposes as indicated is proper.

The requirement is still deemed proper and is therefore made FINAL.

However, because no art was found on the elected species, nor on any of the species, the species requirement has been withdrawn.

Claims 59-79 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 6, filed 11-13-01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

The information disclosure statement filed 11-16-99 (Paper No.3) fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

It is noted that applicant states that these references were cited in the parent of this application where paper copies can be found, and so no copies are attached (MPEP 609). Applicant further states that 09/434,406 which is a continuation of 08/967,242 which is a continuation of 08/374,468. First the examiner notes that no IDS was submitted with said parent 09/434,406. Further the examiner notes that the instant application only claims priority to 08/374,468, and said references that were stated to be submitted with 08/373,468 were not available to the examiner. If applicant wishes the instant IDS statement to be considered, applicant is requested to submit a copy of the cited references.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on applications P4403522.5, P4401629.8 and P4418091.8 filed in DE on 2/4/94, 1/20/94 and 5/24/94, respectively. It is noted, however, that applicant has not filed a certified copy of the three applications as required by 35 U.S.C. 119(b).

It is noted that this application appears to claim subject matter disclosed in prior co-pending Application No. 09/434,406, filed 6-30-99 which is a continuation of 08/967,242, filed 11-5-97, which is a continuation of 08/374,468, filed 1-18-95. A reference to the prior application must be inserted as the first sentence of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a). Also, the current status of all nonprovisional parent applications referenced should be included.

If the application is a utility or plant application filed on or after November 29, 2000, any claim for priority must be made during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2) and (a)(5). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) a surcharge under 37 CFR 1.17(t), and (2) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Commissioner may require additional information where there is a question whether the delay was unintentional. The petition should be directed to the Office of Petitions, Box DAC, Assistant Commissioner for Patents, Washington, DC 20231.

Drawings

New formal drawings are required in this application because of the reasons stated on PTO form 948 attached to the office action mailed 9-27-01 (Paper No. 4). Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the Patent and

Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

C. Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in **ABANDONMENT** of the application.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 46-47, 49 and 51-54and 56 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The instant claims are drawn to a complex comprising a peptide derived from glutamic acid decarboxylase, or derivative thereof, bound to an MHC Class II molecule DR3 or DR4. Since the instant claims when read broadly basically read on any peptide that binds DR3 or DR4 that binds an MHC Class II molecule DR3 or DR4, the instant claims read on complexes found in any human bearing the class II molecules DR3 or DR4. As written, the instant claims read on whole, naturally-occurring complexes. Amending the claims by inserting the word "isolated" before the word "complex" in line 1 of claim 46 would obviate this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A) Claims 46-58 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claims are drawn to a complex or pharmaceutical composition thereof, wherein said complex comprises a peptide or peptide derivative derived from glutamic acid decarboxylase which is bound to an allele or a peptide-binding derivative of MHC Class II molecules DR3 or DR4, wherein said peptide or peptide derivative has a length of at most 25 amino acids and comprises (a) a peptide of at least 6 amino acids of SEQ ID NO:2, or (b) a peptide or peptide derivative having a length of 6-25 amino acids which exhibits a specificity or/and affinity which is essentially equivalent to that of peptide (a) and includes anchor positions for binding to alleles or peptide binding derivatives of MHC Class II molecules DR3 or Dr4.

The instant disclosure of a complex comprising a "a peptide of at least 6 amino acids of SEQ ID NO:2" and "a peptide or peptide derivative having a length of 6-25 amino acids which exhibits a specificity or/and affinity which is essentially equivalent to that of peptide (a)" and "an allele or a peptide-binding derivative of MHC Class II molecules DR3 or DR4" does not adequately describe the scope of each claimed genus, each of which encompasses a substantial variety of subgenera. The instant specification describes no derivative or fragment of the amino acid sequence consisting of SEQ ID NO:2, which consists of 25 amino acids. Further there is inadequate written description for the recitation of the limitation that said peptide includes anchor positions for binding to alleles or peptide-binding derivatives of MHC Class II molecules DR3 or DR4, because there is no description of the required anchor resides which make up the Class II binding motif of said peptides, such as the specific number and specific position of said anchor residues, within a peptide, or such as which specific amino acid can suffice in which

specific anchor positions. It is noted that US-PAT-NO: 5489742 teaches that at least eight subtypes of the alloantigen HLA-DR4 have been identified, including Dw4, Dw10, Dw13.1, Dw13.2, Dw14.1, Dw14.2, Dw15 and Dw "New", (see column 3, lines 13-19). Furthermore, Ramensee et al (Immunogenetics (1995) 41:178-228) teaches that at least 4 of said haplotypes bind peptides that contain distinct sets of consensus binding motifs which contain distinct anchor residues, (see entire article, including pages 213-214). The specification does not describe the motifs for any of said Class II binding peptides, and with the exception of a peptide consisting of the amino acid sequence of SEQ ID NO:2, the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify the polypeptides encompassed. It is noted that a description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly&Co.*, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Therefore, based on the instant description of only one peptide, (a peptide consisting of the amino acid sequence of SEQ ID NO:2) and no description of the requisite number, position and identities of anchor residues of the claimed genus of peptides, the structure of a complex or pharmaceutical composition thereof, wherein said complex comprises "a peptide or peptide derivative derived from glutamic acid decarboxylase which is bound to an allele or a peptide-binding derivative of MHC Class II molecules DR3 or DR4, wherein said complex comprises peptide or peptide derivative having a length of 6 to 25 amino acids, which exhibits a specificity or/and affinity which is essentially equivalent to that of the peptide of at least 6 amino acids of SEQ ID NO:2, and includes anchor positions for binding to alleles or peptide-binding derivatives of MHC class II molecules DR3 or DR4", is not conventional in the art and one of skill in the art would not recognize from the disclosure that applicant was in possession of the genus of said complex comprising said peptides encompassed by the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.)

B) Claims 46-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a complex comprising a peptide or peptide derivative derived from glutamic acid decarboxylase which is bound to an allele or a peptide-binding derivative of MHC Class II molecules DR3 or DR4, wherein said complex comprises "a peptide consisting of the amino acid sequence of SEQ ID NO:2, and includes anchor positions for binding to alleles or peptide-binding derivatives of MHC class II molecules DR3 or DR4, does not reasonably provide enablement for the broader recitation of a complex comprising any peptide or any peptide derivative derived from glutamic acid decarboxylase which is bound to an allele or a peptide-binding derivative of MHC Class II molecules DR3 or DR4, wherein said complex comprises any peptide or any peptide derivative having a length of 6 to 25 amino acids

which exhibits a specificity or/and affinity which is essentially equivalent to that of the peptide of at least 6 amino acids of SEQ ID NO:2, and includes anchor positions for binding to alleles or peptide-binding derivatives of MHC class II molecules DR3 or DR4". The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed in the instant claims without an undue amount of experimentation.The scope of the claims is not commensurate with the enablement provided by the disclosure with respect to the extremely large number of peptides broadly encompassed by the claims.

The instant claims are drawn to a complex or pharmaceutical composition thereof, wherein said complex comprises a peptide or peptide derivative derived from glutamic acid decarboxylase which is bound to an allele or a peptide-binding derivative of MHC Class II molecules DR3 or DR4, wherein said peptide or peptide derivative has a length of at most 25 amino acids and comprises (a) a peptide of at least 6 amino acids of SEQ ID NO:2, or (b) a peptide or peptide derivative having a length of 6-25 amino acids which exhibits a specificity or/and affinity which is essentially equivalent to that of peptide (a) and includes anchor positions for binding to alleles or peptide binding derivatives of MHC Class II molecules DR3 or DR4.

The instant specification discloses no derivative or fragment of the amino acid sequence consisting of SEQ ID NO:2, which consists of 25 amino acids. It is noted that the instant claims recite the limitation that said peptide or peptide derivative, includes anchor positions for binding to alleles or peptide-binding derivatives of MHC Class II molecules DR3 or DR4. However, the specification does not teach the motifs for any of said Class II binding peptides. Ramensee et al teaches the class II binding motifs of 4 DR4 haplotypes (see entire article, including pages 213-214). However, it is noted that US-PAT-NO: 5489742 teaches that at least eight subtypes of the alloantigen HLA-DR4 have been identified, including Dw4, Dw10, Dw13.1, Dw13.2, Dw14.1, Dw14.2, Dw15 and Dw "New", (see column 3, lines 13-19). Therefore there are several peptide motifs, known and unknown, that have not been disclosed. Therefore, it would require undue experimentation for one of skill to predict which peptide fragments and peptide derivatives of SEQ ID NO:2 could bind DR3 or DR4, without further guidance and direction regarding the peptide binding motifs required by the numerous alleles of DR3 and DR4. Further, it is noted that Rammennsee et al al (Immunogenetics (1995) 41:178-228) teaches that at least 12 amino acids are generally necessary to provide the essential motif for peptide binding to MHC Class II molecules (see entire article, including page 183, column 2). The instant claims all encompass complexes comprising peptides which have less than 10 amino acids. Therefore it would require undue experimentation to predict which peptides sequences of which length would bind DR3 or DR4, with the exception of a peptide consisting of the amino acid sequence of SERQ ID NO:2, without further guidance and direction from the instant specification.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, it would take undue trials and errors to practice the claimed invention.

Conclusion

No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy M. DeCloux whose telephone number is 703 306-5821. The examiner can normally be reached on M-F 8:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 703 308-3973. The fax phone numbers for the organization where this application or proceeding is assigned are 703 305-3014 for regular communications and 703 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.

Amy DeCloux, Ph.D.
Patent Examiner,
January 4, 2003

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